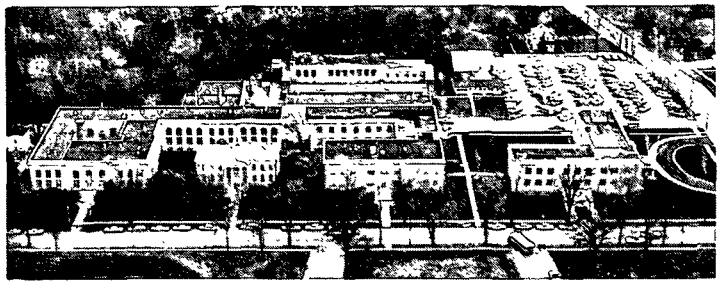

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STEREOSELECTIVE FORMATION OF 1,4-ANHYDRO-2-C-CARBOXYTETRITOLS IN THE DEGRADATION OF 1,5-ANHYDROALDITOLS WITH OXYGEN IN AQUEOUS SODIUM HYDROXIDE SOLUTIONS

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FEBRUARY, 1978

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INTRODUCTION

In recent years, environmental concerns have stirred interest in the use of oxygen and alkali for delignifying and brightening pulps. To take full advantage of these processes, the oxidative degradation of the wood polysaccharides has to be minimized. In the case of cellulose, degradation is manifested primarily as a decrease in viscosity caused by depolymerization. Additives, such as magnesium compounds, can decrease the degradation of carbohydrates to some extent and such "stabilized" processes have the advantage of greatly reducing effluent toxicity while producing pulps with acceptable papermaking properties. In order to increase the prospects for better control of carbohydrate degradation in oxygen-alkali, a workable knowledge of the reaction mechanism is necessary.

This paper is an extension of an earlier paper [IPC Technical Paper Series Number 31; Carbohyd. Res. 56, 259-276 (1977)] which considers the basic questions of how the monomeric pyranoid ring is degraded by oxygen in an alkaline medium and whether the degradation is affected by the stereochemistry of the hydroxyl groups on the ring.

This paper will be submitted for publication in Carbohydrate Research.

Note

Stereoselective Formation of 1,4-Anhydro-2-C-carboxytetritols in the Degradation of 1,5-Anhydroalditols with Oxygen in Aqueous Sodium Hydroxide Solutions

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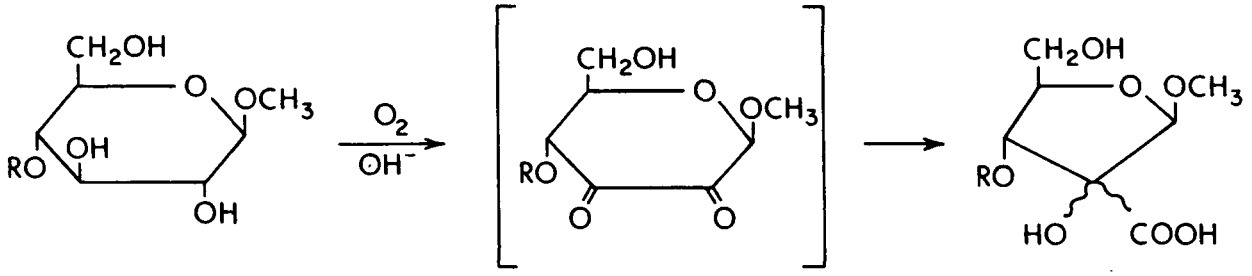
Degradations of methyl β-D-glucopyranoside (1)[1,2], methyl 4-O-methyl-β-D-glucopyranoside (2)[3], and various other methyl glycopyranosides[4] with oxygen in alkaline media yield significant amounts of methyl C-carboxyfuranosides, e.g., 3, which have been postulated to form from α-dicarbonyl intermediates, e.g., 4, by benzilic acid-type rearrangements[1-4].



1 R = H
2 R = CH_3

4

3

During a study of reactions of 1,5-anhydroribitol (5) and 1,5-anhydroxylitol (6) with oxygen in aqueous 1.25N sodium hydroxide at 120°C, diastereomeric 1,4-anhydro-2-C-carboxytetritols (7 and 8) were identified by g.l.c.-mass spectrometry as major products in both reactions[5,6], but definite isomeric assignments could not be made. The carboxytetritols, 7 and 8, are analogous to the carboxyfuranosides 3 formed in reactions of the methyl glycosides. The reactions of

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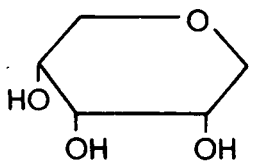
the two anhydroalditols (5 and 6) were similar in that the total concentration of the carboxytetritol products (7 and 8) went through a maximum in both systems. However, distinct differences in the ratio of the isomeric carboxytetritols as the reactions progressed were evident, as illustrated by the series of chromatographic analyses shown in Figure 1 in which the unassigned diastereomers are labelled simply as A and B*.



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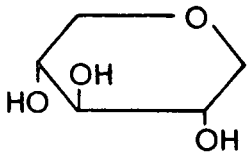

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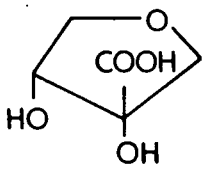

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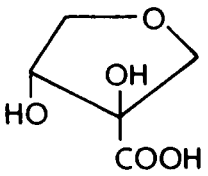

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[Fig. 1 here]

Initially, carboxytetritol B dominated in the reaction of 1,5-anhydroribitol (5), but it became increasingly less important as the reaction progressed. Conversely, throughout the reaction of 1,5-anhydroxylitol (6), the dominant carboxy tetritol product was A. As the reaction of 6 proceeded, the relative amount of B continually decreased to where it was not detectable chromatographically. The data indicate that carboxytetritol A is formed preferentially in the anhydroxylitol (6) reaction while carboxytetritol B is selectively formed in the anhydroribitol (5) reaction. Also, it is apparent that B reacts more rapidly than A to form other products under these reaction conditions.

If the reactions of 5 and 6 to form A and B proceeded solely through α-dicarbonyl intermediates as postulated for analogous glycosidic reactions[1-4], the differences in the ratios of A and B formed in the two reactions would not be expected since the α-dicarbonyl species which can form from 5 and 6 are identical.

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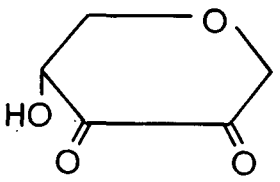
*Each diastereomeric product is probably a mixture of the D and L enantiomers.

The two intermediates which could be formed from either 5 or 6 are the enantiomers 9 and 10. Thus, while the α-dicarbonyl compounds (9 and 10) may be intermediates



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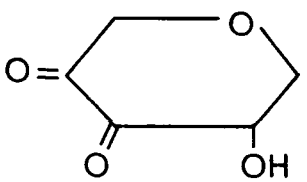

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in the reactions of 5 and 6, they cannot be exclusive. Other reaction intermediates which have a stereochemical directing effect because of the configuration of substituents at C-3 must be important to account for the observed differences in formation of the diastereomeric carboxytetritol products.

Potential reaction schemes which account for stereoselective formation of diastereomeric carboxytetritols in reactions of 5 and 6 are shown in Figures 2 and 3. The initial step of both reactions is postulated to be oxidation of a hydroxyl group to a carbonyl group via an α-hydroxyhydroperoxide as discussed previously[5,6]. The reactions are illustrated for initial oxidation at C-2; initial oxidation at C-4 would produce the enantiomeric product. Initial oxidation at C-3 is possible, but would produce identical intermediates from 5 and 6, thereby eliminating any potential for different ratios of 7 and 8 to be formed from the two anhydroalditols.

[Fig. 2 and 3 here]

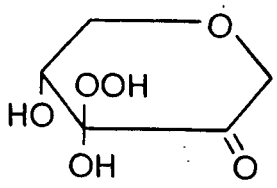
The next step postulated for both reactions is reversible addition of hydroxide ion to the carbonyl group. In both systems, the species in which the oxyanion of the resulting gem-diol is cis to OH-3 (11 and 11a) should be stabilized by effective hydrogen bonding as illustated[5]. Abstraction of H-3 from 11 or 11a by any of several radical species (R·) in the system[5] would

produce a hydroxyalkyl radical at C-3 (12 and 12a). Stereoselective addition of oxygen to 12 and 12a to form the α-hydroxyhydroperoxyl radicals 13 and 13a, respectively, would be facilitated by stabilization of the C-3 radical to inversion by the hydrogen bonding. In addition, reaction of the hydroxyalkyl radicals (12 and 12a) with oxygen would be very rapid since it would be expected to have an essentially zero activation energy[7-9]. The hydroperoxyl radicals 13 and 13a would readily abstract hydrogen atoms from other substrates to form the key α-hydroxyhydroperoxide intermediates, 14 or 14a, which in the alkaline medium should readily form the conjugate bases of the hydroperoxides, 15 and 15a, also.

The carboxytetritols 7 and 8 could be formed readily from 14 and 14a or 15 and 15a, respectively, by a semibenzilic type mechanism[10,11]. Transfer of the hydroxyl proton to the peroxy anion of 15 and 15a could precede or be concerted with the ring contraction. Formation of the carboxylic acid carbonyl moiety would be concerted with ring contraction and displacement of the hydroperoxy anion as shown in Figures 2 and 3. The concerted rearrangements must occur from the conformations [C_1^4 (D) for 5 and C_4^1 (D) for 6] in which the (C-1)-(C-2) bond and the carbon-oxygen bond of the hydroperoxide are anti-periplanar. In the conformation necessary for rearrangement, the bulky hydroperoxide group is equatorial, thus helping to stabilize the molecule in that conformation.

Naturally, the potential exists for the α-hydroxyhydroperoxide moiety of 14, 14a, 15, or 15a to form a carbonyl group[5] prior to the ring contraction, thus forming the α-dicarbonyl species (or its hydrate) which could undergo a benzilic acid type rearrangement. In those reactions in which this occurs, the proportion of 7 and 8 formed from the anhydroalditols 5 and 6 would be the same.

Compounds 14 and 15 can also potentially exist in equilibrium with 16. Similarly 14a and 15a could exist in equilibrium with 16a. Thus, the Favorskii



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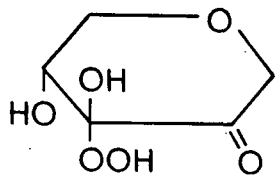


16a

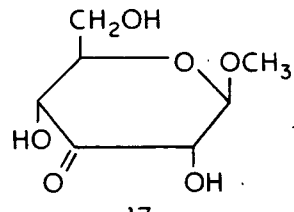
reaction[10,11] involving 16 and 16a was also considered for formation of 7 and 8. This would involve initial formation of a carbanion at C-1 and subsequent migration of C-1 to C-3 with displacement of the hydroperoxy anion from C-3 to form the cyclopropanone intermediate. Ring-opening of the cyclopropanone intermediates to form C-1 carbanions would result in formation of the 1,4-anhydro-2-C-carboxytetritols (7 and 8). Because of potential elimination reactions, alternate ring-opening of the cyclopropanone intermediates would yield several compounds, none of which were found in the product mixtures.

However, the Favorskii mechanism does not appear to be as viable as the semibenzilic mechanism for the formation of 7 and 8. For example, if a C-1 carbanion did form, it would be expected to undergo inversion. Carbanions stabilized by adjacent carbonyl groups usually give racemization no matter what the solvent[11,12]. While inversion of the C-1 carbanion would not affect the final products in reactions of 5 and 6, in glycosidic systems carbanion inversion would result in formation of anomeric mixtures of the alkyl C-carboxyfuranosides. Such anomeric product mixtures have not been reported[1-4].

The mechanisms shown in Figures 2 and 3 predict that 7, 1,4-anhydro-2-C-carboxy-D-erythritol and its L-enantiomer would form preferentially in reactions

of 1,5-anhydroribitol (5) while 8, 1,4-anhydro-2-C-carboxy-D-threitol and its L-enantiomer would form preferentially in reactions of 1,5-anhydroxylitol (6). On this basis carboxytetritol A (Figure 1) would be 8, the threitol isomer, while B, the isomer which degrades most rapidly would be 7, the erythritol isomer. This is consistent with observations that carbohydrates having cis vicinal hydroxyl groups are more reactive than the trans isomers with oxygen in aqueous alkali[4,5].

In contrast to the proposed mechanisms, Ericsson, et al.[1,2] have questioned the importance of monocarbonyl species as precursors to C-carboxyfuranoid species. Since glycosiduloses, e.g., 17 and 18, are extremely labile in alkaline solution[13,14], it was postulated that for the reaction of methyl β-D-glucopyranoside with oxygen in alkali, the α-dicarbonyl intermediate, i.e., 4, must be formed by simultaneous introduction of the two carbonyl groups[2]. However, on reaction with oxygen in aqueous alkali, methyl β-D-ribo-hexopyranosid-3-ulose (17), which eliminates the aglycon more rapidly[13,14] and is probably less likely to form initially than the 2-ulose (18), formed 35-65% of the C-carboxyfuranosides generated from methyl β-D-glucopyranoside under comparable conditions[1,2]. Thus it would seem that postulating monocarbonyl species as intermediates in these types of oxidations is not unrealistic.



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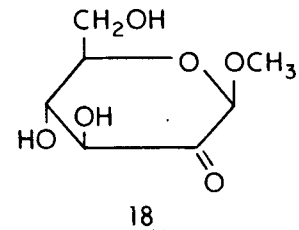

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The experimental aspects of this study have been reported in detail elsewhere[5,6].

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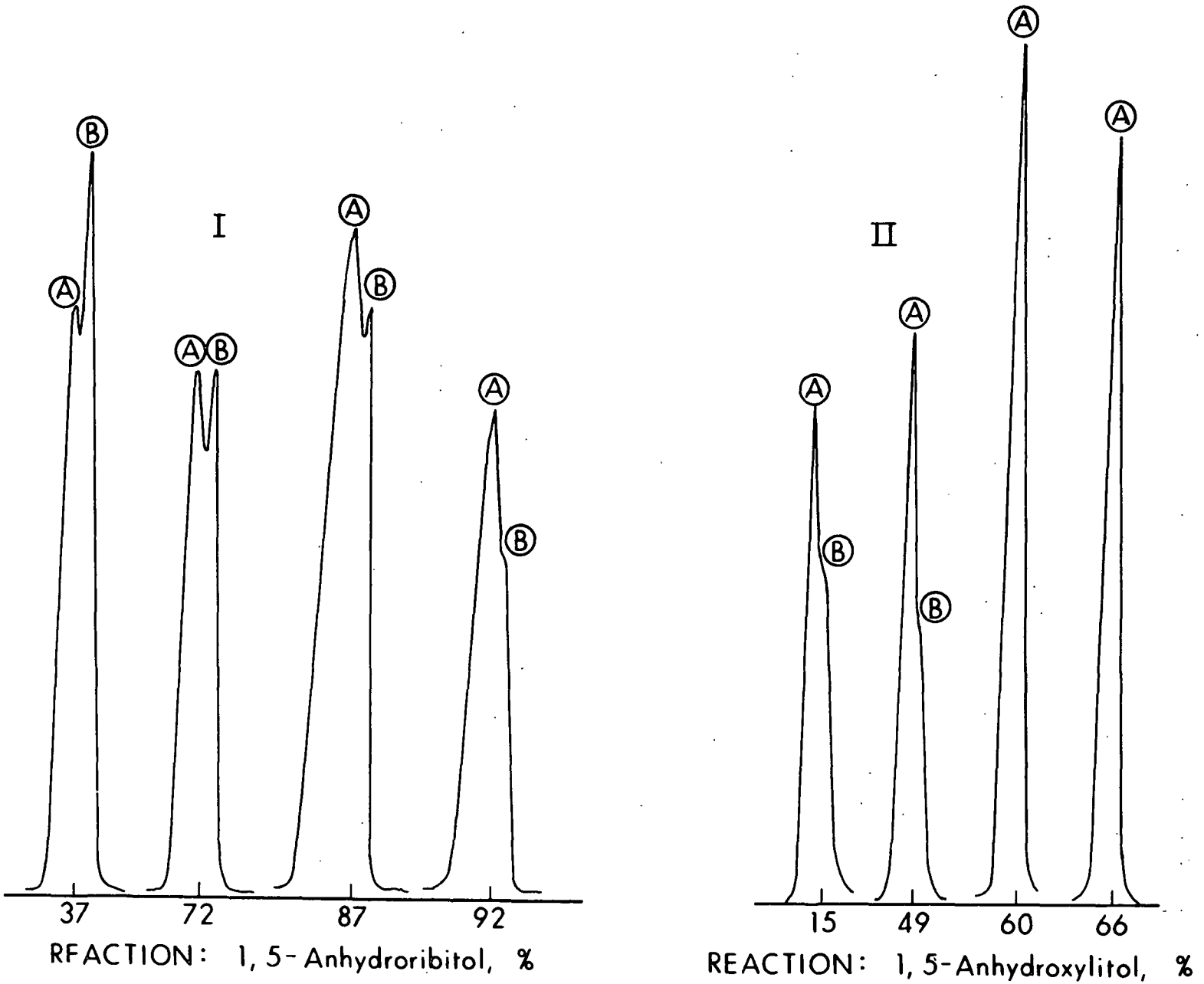

Figure 1. Gas-Liquid Chromatographic Analysis of Diastereomeric 1,4-Anhydro-2-C-carboxytetritols (Me_3Si Derivatives) Formed in the Reactions of 1,5-Anhydroribitol (I) and 1,5-Anhydroxylitol (II).

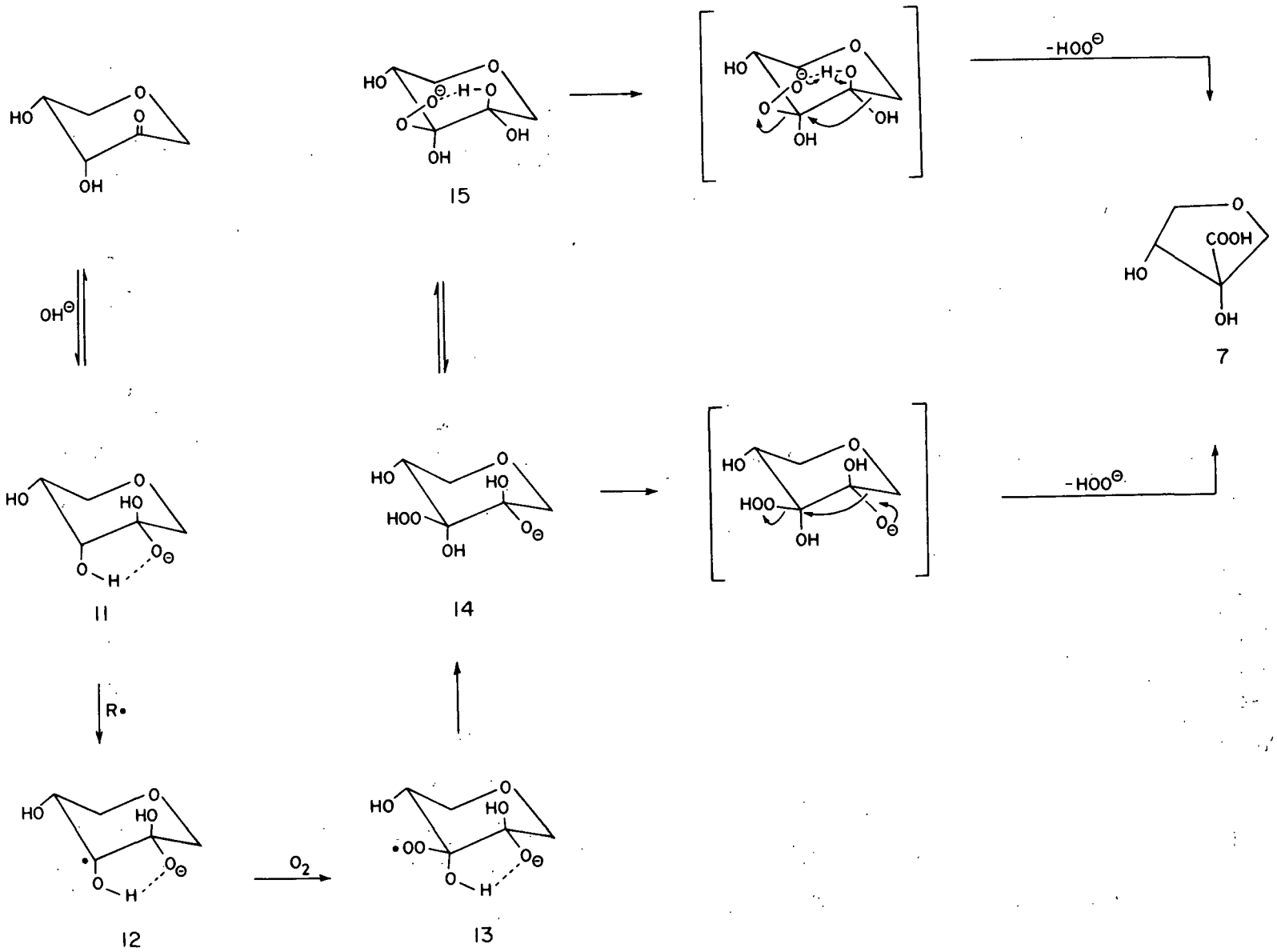

Figure 2. Suggested Mechanism for Stereoselective Formation of 1,4-Anhydro-2-C-carboxy-D-erythritol from 1,5-Anhydroribitol.

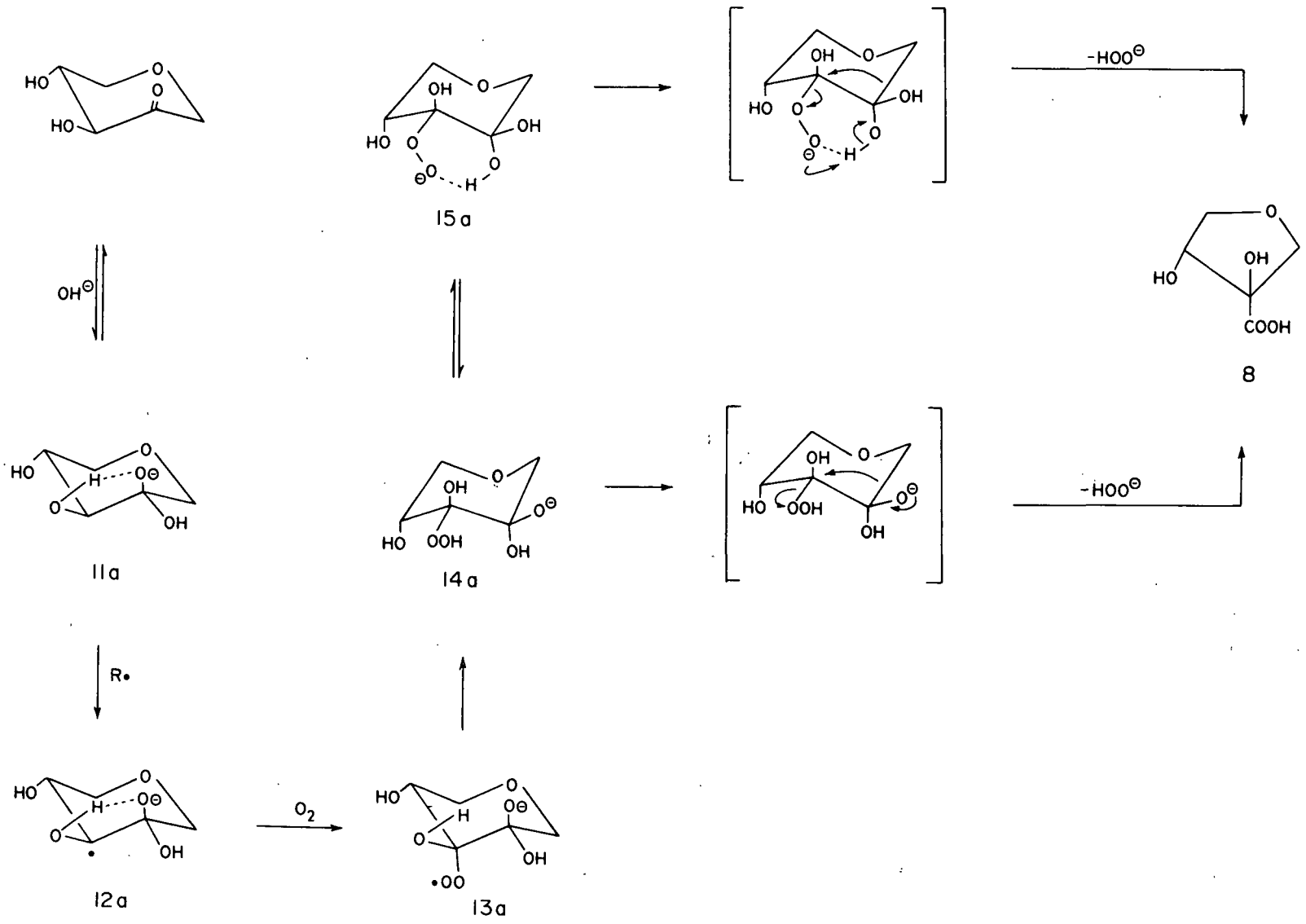

Figure 3. Suggested Mechanism for Stereoselective Formation of 1,4-Anhydro-2-C-carboxy-D-threitol from 1,5-Anhydroxylitol.